
بسم الله الرحمن الرحيم
السلام عليكم ورحمة الله وبركاته



Armed Forces College of Medicine

AFCM



Analgesic Antipyretics

(3)

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. Identify the most important pharmacological differences between aspirin and other NSAIDs
2. Explain the mechanism of analgesic and antipyretic actions of Acetaminophen (Paracetamol)
3. Identify the therapeutic uses of Paracetamol
4. Relate the metabolism of paracetamol to its acute toxicity
5. Recognize Choice of drugs in treatment of Rheumatoid arthritis

Other Non-Selective COX – Inhibitors

- **Ibuprofen, ketoprofen, Naproxen**

  less Gastric irritation and bleeding

- **Indomethacin**

Very Potent Analgesic Anti-pyretic –inflammatory Rheumatic.

but severe side effects (aplastic anaemia)

- **Mefenamic acid (ponstan)**

  severe *diarrhea* & abdominal pain.

  Not More than a week. **NOT** in Children or Pregnancy

Selective *COX-2 Inhibitors* (Coxibs)

- **They Include:**

♦ Celecoxib

Extensively Metabolized in the liver by cytochrome P-450



Selective *COX-2 inhibitors*

Cytoprotective PGs

Less G.I.T. irritation

No effect on platelets

Less renal toxicity

(Cox-2 is constitutive in the kidney)

Inflammatory PGs

Analgesic

Anti-Pyretic

Anti-Inflammatory

Selective *COX-2 inhibitors*

Side Effects

- High incidence of thrombo-embolic diseases

Acetaminophen (Paracetamol)

Acetaminophen

Selective

COX-3

Mainly C.N.S

Analgesic

Anti-Pyretic

Weak Peripheral Action

No Anti-inflammatory

No effect on:

- Gastric acidity
- Platelet aggregation
- Bronchial asthma
- Uric acid.

Acetaminophen

Uses:

Analgesic Antipyretic (1/2 – 1 g)

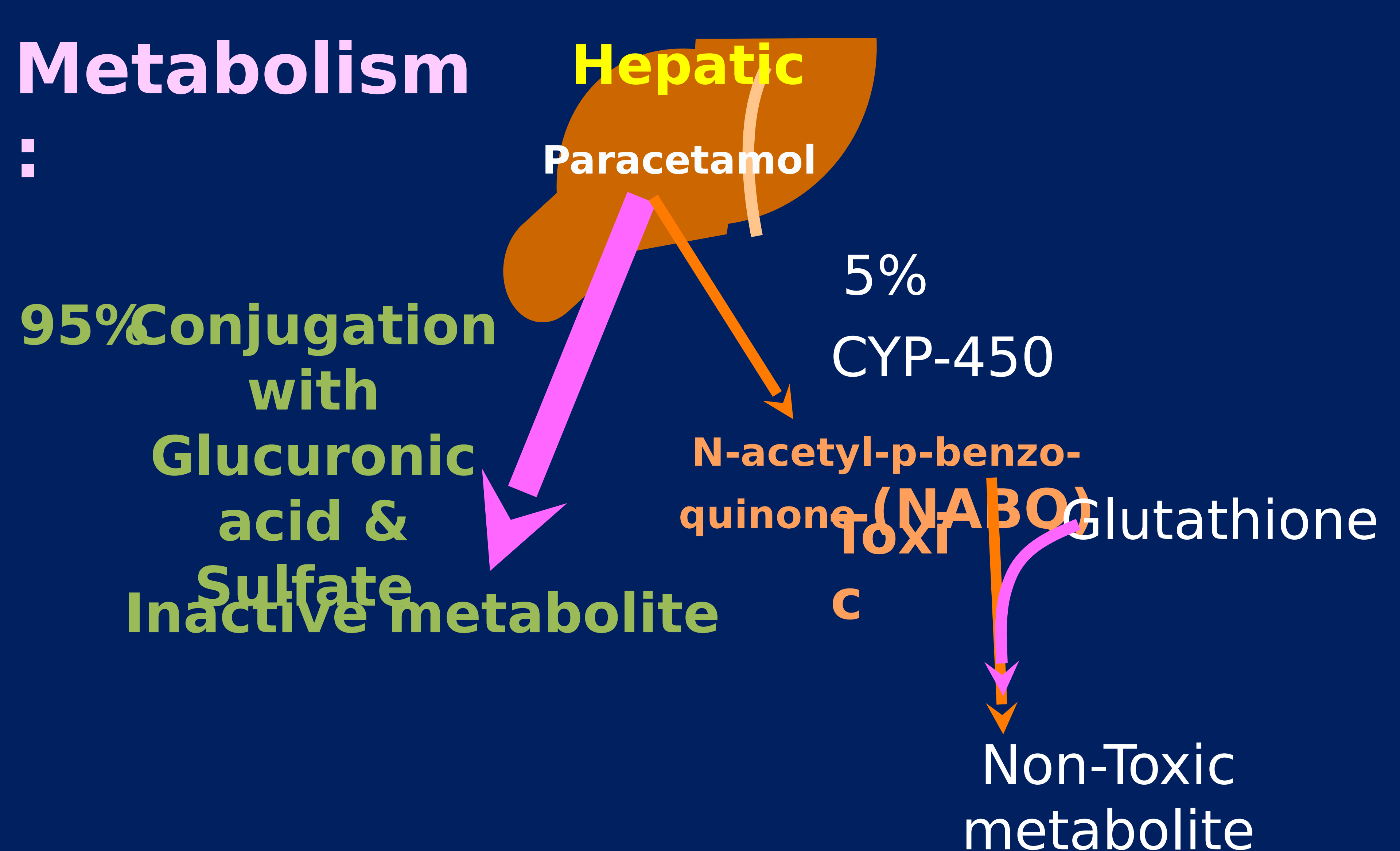
especially in patients who can not tolerate aspirin e.g.

- Allergy to Aspirin,
- Bronchial asthma,
- Peptic ulcer
- Children with viral infection,
- Bleeding tendency
- Gout.

All of the following can be produced by acetaminophen EXCEPT:

a) Anti-inflammatory effect
b) Analgesic effect
c) Anti-pyretic effect
d) Inhibition of COX-3 enzyme
e) Liver damage on overdose

Acetaminophen (Paracetamol)



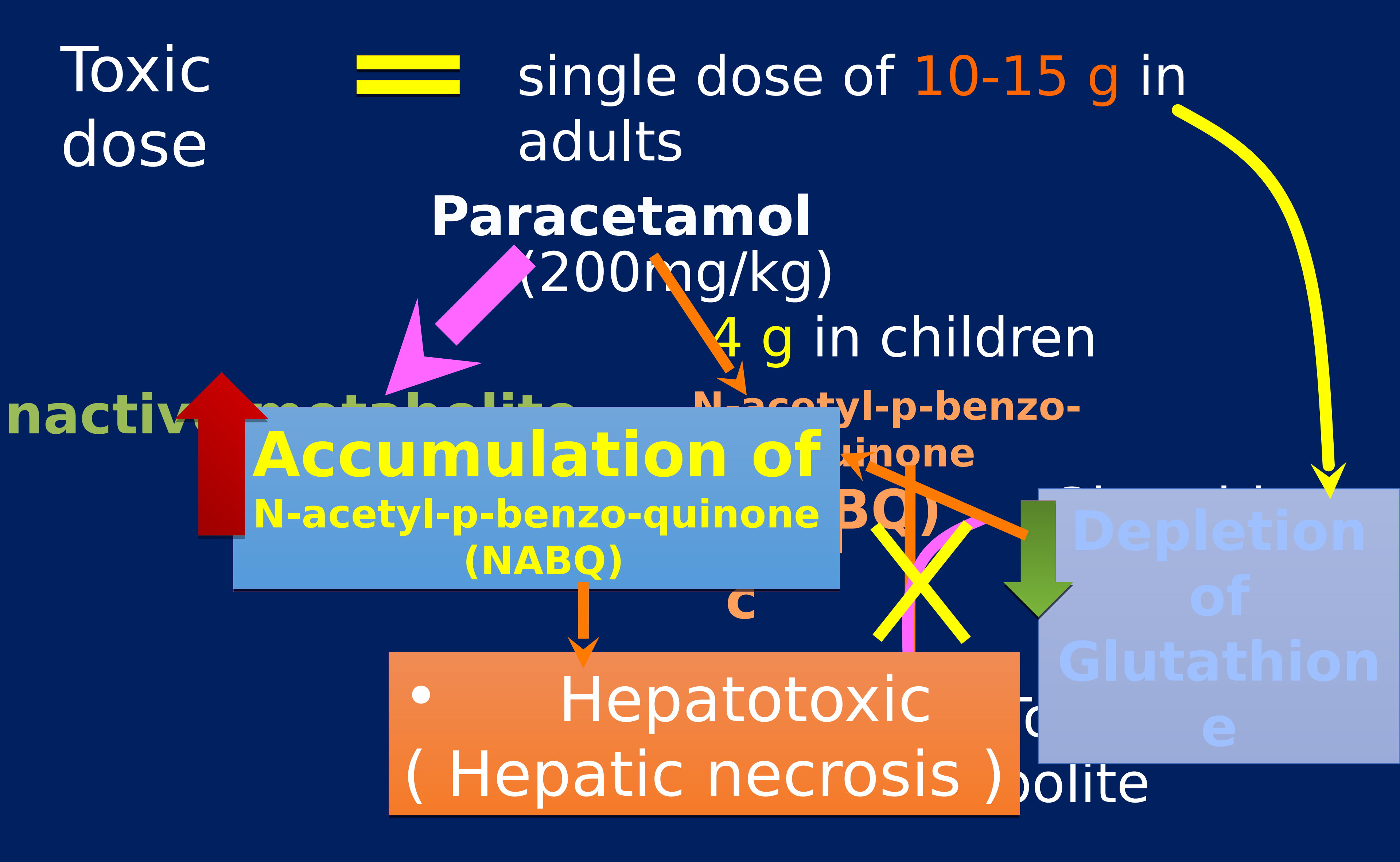
Acetaminophen

Adverse effects:

It is well tolerated at therapeutic doses.

if toxic dose □ Hepatic necrosis

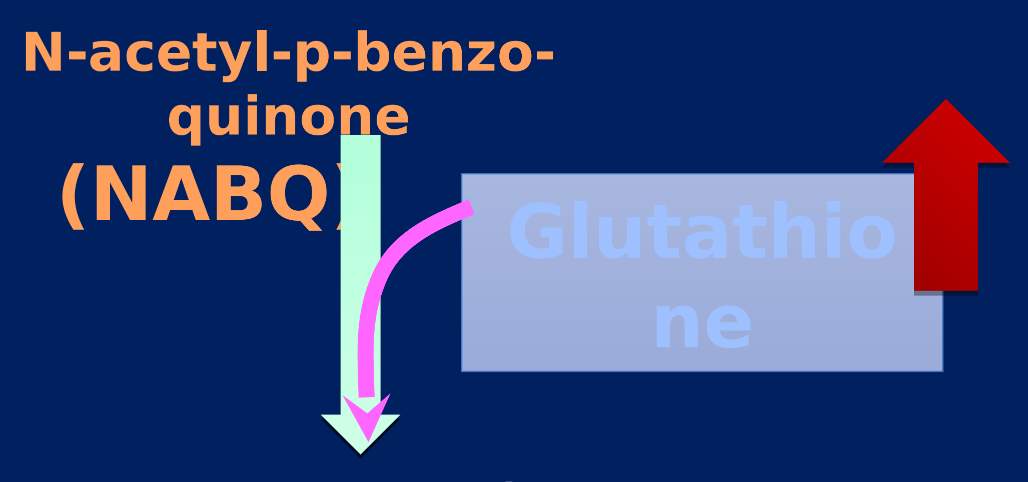
Acetaminophen ➢ **Acute Toxicity:**



Acetaminophen ➢ **Acute Toxicity:**



N-Acetylcysteine I.V (Rich in S-H)



Non-Toxic metabolite

Treatment of Rheumatoid Arthritis

I- Steroidal Anti-Inflammatory Drugs (SAIDs):

e.g. corticosteroids as Prednisolone.

II- Non-Steroidal Anti-Inflammatory Drugs:

A) Rapidly Acting Anti-Rheumatic Drugs:

Almost All Antipyretic Analgesics *Exce*

Paracetamol

B) SLOW Acting Anti-Rheumatic Drugs:

Disease Modifying Anti-Rheumatic Drugs (DM-ARD)

slow the course of the disease, **induce remission**,
and **prevent further destruction** of the joints and
involved tissues.

➢ **When a patient is diagnosed with RA:**
DMARDs should be started within 3 months to help
stop the progression of the disease at the earlier
stages.

Choice of drugs in treatment of Rheumatoid Arthritis

- **For patients with low disease activity:**

  Monotherapy may be initiated **with any of the DMARDs**

  (methotrexate, leflunomide, hydroxychloroquine,or sulfasalazine)

  No one DMARD is efficacious and safe in every patient, and trials of several different drugs may be necessary.

- **For patients with moderate to high disease activity or inadequate response to monotherapy:**

  Combination DMARD therapy (usually methotrexate based)

  OR

  Use of **anti-TNF drugs** (e.g adalimumab,etanercept and infliximab)

An 18-month-old boy dies from an accidental overdose of acetaminophen. Which of the following is the most likely cause of this patient's death?

a) Arrhythmia
b) Hemorrhagic stroke
c) Liver failure
d) Non cardiogenic pulmonary edema
e) Ventilatory failure

- **Ibuprofen, ketoprofen, Naproxen: less Gastric irritation and bleeding**
- **Mefenamic acid (ponstan)** severe *diarrhea* & abdominal pain.

NOT in Children or Pregnancy

- **Indomethacin** Very Potent *but severe side effects (aplastic anaemia)*
- **Diclofenac (voltaren) :** ***Concentrated in synovial fluid 4 times > plasma***

Acetaminophen (Paracetamol)

1. Acetaminophen (Paracetamol) has analgesic and antipyretic actions
2. Acetaminophen has **NO anti-inflammatory action**
3. Acetaminophen acts by **selective inhibition of COX-3 enzymes**
4. Paracetamol **acute toxicity is due to Accumulation of N-acetyl-p-benzo-quinone (NABQ) metabolite which is toxic to the liver** and results in Hepatic

Suggested Textbooks



1. Whalen, K., Finkel, R., & Panavelil, T. A. (2018) Lippincott's Illustrated Reviews: Pharmacology (7th edition.). Philadelphia: Wolters Kluwer

2. Katzung BG, Trevor AJ. (2018). Basic & Clinical Pharmacology (14th edition) New York: McGraw-Hill Medical.

Thank You